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Opportunistic Testing: The Death of Informed Consent?

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OPPORTUNISTIC TESTING: THE DEATH OF INFORMED CONSENT?

Dena S. Davis[†]

ABSTRACT

This Article focuses on one aspect of prenatal diagnosis: noninvasive prenatal diagnosis, particularly the detection of Trisomy 21 (Down Syndrome) through a simple test of maternal blood. Although I discuss issues salient to this particular test, I place it in the context of “opportunistic” testing generally. It is my view that opportunistic testing presents the most serious challenge to patient autonomy we are facing in the twenty-first century. In this Article, I will explain what I mean by opportunistic testing¹ and consider three different examples of how it threatens informed consent: (1) Prostate-Specific Antigen (PSA) screening, (2) newborn screening, and (3) prenatal diagnosis of maternal blood tests for fetal anomalies.

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1. In this Article, I use the terms “testing” and “screening” interchangeably because my three examples encompass both activities. Technically, however, screening describes evaluation of people who have no symptoms, to uncover a possible problem or risk factor; testing is part of a diagnostic evaluation in response to a symptom. In genetic medicine, screening usually describes a wide program that captures a broad population, while testing can target a small population or single person known to be at higher risk. Often the same modality (e.g., a mammogram) can be used as a screen or as a diagnostic test.

I. OPPORTUNISTIC TESTING

Opportunistic testing or screening is medical testing that makes use of an “opportunity” engendered by some other test or modality to which the patient² is accustomed or has already given consent. The opportunity could be as simple as the patient presenting herself for some other reason, as in screening asymptomatic patients for an STD such as chlamydia.³ In this context, the term opportunistic always implies “piggybacking” one intervention onto another and thus exploiting an opportunity. It does not necessarily imply lack of transparency. An opportunistic intervention can be an obviously different event, as when patients in a general practice waiting room who had made appointments for complaints unrelated to depression were screened for depression with their informed consent.⁴

Because opportunistic interventions are, by definition, performed on patients who are presenting for a different reason, they are often associated with preventive care.⁵ As prevention becomes an increasingly important medical concept and recommendations for preventive measures grow exponentially, some critics are beginning to question the dilution of focus on the patient’s reason for coming to the medical setting and the imposition of risk information the patient may not want. As one commentator notes, “once information about medical risk has been passed on to a person . . . it cannot be retracted. Respect for autonomy should therefore also honour the person’s right not to be opportunistically confronted with knowledge about biomedical risks that are unrelated to his or her reasons for seeing the doctor.”⁶

This Article focuses on a particular subset of opportunistic testing, namely tests done on a blood sample. In this case, the blood sample is drawn for an established purpose and then one or more extra tests are added. From the patient’s perspective, the intervention (a heel prick or blood draw) is exactly the same, making it easy for a medical professional to add extra tests without the patient’s consent or knowledge. If the

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2. I dislike the word “patient” for many reasons, not least its implication of passivity. Nonetheless, there seems no better term. I prefer the locus of control implied by “health care consumer” or even “client,” but those terms do not capture the long history of the doctor/patient relationship from which bioethics draws.
 3. Cliodna A. M. McNulty et al., *Barriers to Opportunistic Chlamydia Testing in Primary Care*, 54 BRIT. J. GEN. PRACTICE 508, 508 (2004).
 4. Matthijs van den Berg et al., *Cost-Effectiveness of Opportunistic Screening and Minimal Contact Psychotherapy to Prevent Depression in Primary Care Patients*, 6 PLOS ONE, Aug. 2011, at 1, 2.
 5. Linn Getz et al., *Is Opportunistic Disease Prevention in the Consultation Ethically Justifiable?*, 327 BRIT. MED. J. 498, 498 (2003).
 6. *Id.* at 499.

result is negative, the patient may never know that the test was performed.

II. PSA SCREENING

Prostate-specific antigen (PSA) is a protein produced by the prostate gland.⁷ A very small amount escapes into the bloodstream, allowing for simple testing by blood sample.⁸ PSA can be used as a screening device for men not known to have prostate cancer or as a test to monitor men who have been treated for prostate cancer.⁹ As H. Gilbert Welch writes,

Like all other efforts to diagnose disease early, cancer screening is a double-edged sword. It can produce benefit: providing the opportunity to intervene early can reduce the number of deaths from cancer. It can produce harm: overdiagnosis and overtreatment. And it can do both at the same time. So while a strong case can be made for cancer screening, there are good reasons to approach it cautiously.¹⁰

PSA screening is especially difficult to assess. On one hand, prostate cancer is the second most common cause of cancer death in men.¹¹ On the other hand, most prostate cancer is “indolent,” causing no symptoms or harm.¹² Most men diagnosed with prostate cancer die *with* the disease than *because of* it.¹³ A number of studies looked for prostate cancer in men who had died of other causes and who were unaware that they had prostate cancer. Forty percent of the men in their forties and 80 percent of men in their seventies were found to have had asymptomatic prostate cancer.¹⁴ A common problem with cancer screening is that it cannot distinguish between three categories of cancer: (1) nonprogressive or very slow-growing cancers for which treatment is unnecessary and even

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7. NAT'L CANCER INST., FACT SHEET: PROSTATE-SPECIFIC ANTIGEN (PSA) TEST 1 (2012), http://www.cancer.gov/cancertopics/factsheet/detection/Fs5_29.pdf [hereinafter PSA FACT SHEET].
 8. *See id.*
 9. *See id.*
 10. H. GILBERT WELCH ET AL., OVERDIAGNOSED: MAKING PEOPLE SICK IN THE PURSUIT OF HEALTH 45 (2011).
 11. Nat'l Cancer Inst., *Prostrate Cancer Screening: Significance*, CANCER.GOV, <http://www.cancer.gov/cancertopics/pdq/screening/prostate/HealthProfessional/page2/AllPages#2> (last updated Oct. 5, 2012).
 12. *See* WELCH ET AL., *supra* note 10, at 45.
 13. *See id.* at 47-48.
 14. *Id.* at 48.

harmful; (2) cancers that are so aggressive that treatment is pointless; and (3) cancers for which treatment will make a difference.¹⁵

Treatment for prostate cancer is hardly harmless: substantial numbers of men who receive surgery or radiation for prostate cancer will experience irreversible impotence, incontinence, or both.¹⁶ The European Randomized Study of Screening for Prostate Cancer, which followed men for eleven years, found that annual PSA screening for men between the ages of fifty-five and sixty-nine reduced mortality from prostate cancer by 28 percent; but when the statistics were calculated as a function of Quality of Life Years, the advantage of screening disappeared.¹⁷ Lives prolonged were canceled out by loss of quality of life. The study found that ninety-eight men would need to be screened and five cancers detected to prevent one death from prostate cancer.¹⁸ Of course, the other four men would almost certainly have received some form of (unnecessary) therapy with a high likelihood of being left with incontinence, impotence, or both.

All reputable sources echo the recommendation from the American Cancer Society that men should “have a chance to make an informed decision with their health care provider about whether to be screened for prostate cancer.”¹⁹ “This decision should be made after getting information about the uncertainties, risks, and potential benefits of prostate cancer screening,” and men “should not be screened unless they have received this information.”²⁰ The National Institutes of Health website advises that the value of PSA screening is “debated” and recommends that men discuss with their doctors the reasons for and against having the test before making a decision.²¹ In 2012, the independent United States Preventive Services Task Force (USPSTF) advised against routine screening for men of any age group.²² Co-Chair Michael Lefevre

15. *Id.* at 53-54.

16. Nat'l Cancer Inst., *Prostate Cancer Treatment (PDQ): Treatment Option Overview*, CANCER.GOV, <http://www.cancer.gov/cancertopics/pdq/treatment/prostate/HealthProfessional/page4> (last modified Sept. 21, 2012).

17. Evelyn A.M. Heijnsdijk et al., *Quality-of-Life Effects of Prostate-Specific Antigen Screening*, 367 NEW ENG. J. MED. 595, 599 (2012).

18. *Id.* at 600.

19. *Can Prostate Cancer Be Found Early?*, AM. CANCER SOC'Y, <http://www.cancer.org/Cancer/ProstateCancer/DetailedGuide/prostate-cancer-detection> (last updated Sept. 4, 2012).

20. *Id.*

21. Nat'l Inst. of Health, *PSA*, MEDLINEPLUS, <http://www.nlm.nih.gov/medlineplus/ency/article/003346.htm> (last updated Sept. 22, 2012).

22. David Mitchell, *USPSTF Recommends Against PSA-based Prostate Cancer Screening*, AM. ACAD. OF FAMILY PHYSICIANS (Oct. 12, 2011, 5:00

explained that “for every 1,000 men treated for prostate cancer, five die of perioperative complications; 10-70 suffer significant complications but survive; and 200-300 suffer long-term problems, including urinary incontinence, impotence or both.”²³ That’s a lot of harm for a cancer that didn’t need to be treated in the first place.”²⁴ Even Dr. Richard Ablin, who discovered PSA in 1970, wrote in 2010 that “[t]he test’s popularity has led to a hugely expensive public health disaster.”²⁵

Many older men continue to be screened despite 2008 USPSTF recommendations against routine PSA screening for men older than seventy-five.²⁶ In fact, it is extremely common for men to be tested without their knowledge. The reason for that lies largely with the opportunistic quality of the test: men are used to having their blood screened at routine visits (e.g., for lipids), and physicians can piggyback the PSA test on top of the other tests without getting extra blood or performing any other action requiring explanation or permission.

While that practice is indefensible, it is easy to imagine the physician’s thought process, or perhaps that of the institution. To not offer PSA might lead to a lawsuit down the road. To offer it with an appropriate discussion would take time, at least fifteen to twenty minutes.²⁷ According to one study, the average office visit lasts 19.3 minutes.²⁸ Physicians and institutions may find it more efficient to give the test to everyone and save time by discussing it only in the 5 percent of cases when the results are problematic.

An individual’s decision about whether to participate in PSA screening should not be regarded as trivial. The professional who offers a test carries a considerable responsibility, because informed consent presupposes an understanding of the limitations of the program. Every test carries a chance of misclassification of disease and false positive results that can lead to further, potentially harmful interventions. In addition, negative results can give false reassurance.

PM), <http://www.aafp.org/online/en/home/publications/news/news-now/health-of-the-public/20111012psascreenrec.html>.

23. *Id.*

24. *Id.*

25. Richard J. Ablin, *The Great Prostate Mistake*, N.Y. TIMES, March 10, 2010, at A27.

26. Sandip M. Prasad et al., *2008 US Preventive Services Task Force Recommendations and Prostate Cancer Screening Rates*, 307 JAMA 1692, 1693 (2012).

27. Telephone Interview with Jonathan Katz, M.D. (June 18, 2012).

28. *Average Doctor Visit Grows -- by 32 Seconds over 10 Years*, WORLD NEWS & NURSING RPT. (Sept. 1, 2007), <http://www.asrn.org/journal-world-news-nursing-report/7-average-doctor-visit-grows-by-32-seconds-over-10-years.html>.

Furthermore, patients and doctors tend to make different choices depending on the way statistical estimates of potential medical benefit are presented. While “a fifty-five-year-old man may, for instance, be interested in an 18 percent reduction in the relative risk of dying from colorectal cancer” with screening, he may be “more reluctant if told that screening implies an absolute risk reduction of only 0.014 percent a year.”²⁹ Alternatively, he may “consider that the likelihood of not dying from colorectal cancer is 99.34 percent if you are screened and 99.20 percent if you are not screened. Unless the doctor is willing to solve this information dilemma by using a simple paternalistic reminder such as, ‘take the test, it is good for you,’ many preventive interventions seem too complex to suit the model of opportunistic health promotion in the general practitioner’s office.”³⁰

Considering the controversy swirling around PSA testing, it is outrageous that so many patients are subjected to it without their knowledge or consent. It is difficult, however, to document what percentage of patients is given the opportunity to make an informed choice before engaging in PSA testing. In 2010, researchers in the United Kingdom reported that only about a third of 106 men given a PSA test were aware of such basic facts as the goals of the test and the likelihood that it would lead to further testing.³¹ The report does not address whether the men were even told that a PSA had been ordered. It appears that men who do undergo an informational process are significantly less likely to express interest in PSA testing than those who were not given that opportunity.³²

A 1999 study in the United States found that one-third of patients at a primary care clinic were “unaware that they had received a screening PSA test, and among patients who were aware of having the test done, fewer than half recalled having a discussion about the associated benefits and risks.”³³ The study further found that “most men did not know that treatment of localized prostate cancer has not been shown to increase survival and can lead to impotence and incontinence. The results indicate that, in most cases, the process of verbal informed consent between patients and health care providers was either ineffective or not done.”³⁴

29. Getz et al., *supra* note 5, at 499.

30. *Id.*

31. See Ashok R. Gunawardene & Mark Kitchen, *Informed Consent for PSA Testing: An Outpatient Audit*, 8 INT’L J. SURGERY 577, 577 (2010).

32. Andrew M.D. Wolf et al., *The Impact of Informed Consent on Patient Interest in Prostate-Specific Antigen Screening*, 156 ARCHIVES INTERNAL MED. 1333, 1334 (1996).

33. Daniel G. Federman et al., *Informed Consent for PSA Screening: Does It Happen?*, 2 EFFECTIVE CLINICAL PRAC. 152, 154 (1999).

34. *Id.* at 155.

In short, PSA testing is a medical intervention on which reasonable minds can differ but which certainly fulfills the ethical criteria for requiring informed consent. Taking the test might save your life. Taking the test might lead to unnecessary treatment with significant and irreversible side effects. Medical organizations urge that physicians discuss the pros and cons of PSA testing with individual patients. Yet significant percentages of patients are given the test without their consent because the test is opportunistic.

III. NEWBORN SCREENING

State-mandated newborn screening began in the 1960s by targeting phenylketonuria (PKU).³⁵ In some places, newborn screening is still referred to as “the PKU test.”³⁶ In this genetic condition, a baby is born without the ability to break down the amino acid phenylalanine.³⁷ Babies with PKU become irreversibly developmentally delayed on a normal diet, but they can progress normally if put on a strict diet that excludes phenylalanine.³⁸ Because early intervention (before symptoms become apparent) is crucial and an effective intervention exists, PKU remains the “poster child” of a successful newborn screening program.³⁹

For some time after PKU screening began, other tests were slowly added. In the past, screening for each new condition required an entirely different test and different lab equipment. Given the tremendous expense of testing all newborns in a state and the relatively small number of children identified, each new test had to surmount a rigorous test of its own in order to be adopted. This slow progression “changed with the invention of tandem mass spectrometry, which allows for ‘multiplex testing’ on the same blood sample for many conditions at once.”⁴⁰ Mass spectrometry has “allowed for unprecedented expansion of newborn screening.”⁴¹ The DNA chip, “already in use in the private sector, will soon make possible additional, exponential expansion of [newborn

35. See Simone Van Der Burg & Marcel Verweij, *Maintaining Trust in Newborn Screening: Compliance and Informed Consent in the Netherlands*, 42 HASTINGS CTR. REP. 41, 41 (2012).

36. See *id.*

37. Nat’l Inst. of Health, *Phenylketonuria*, MEDLINE PLUS, <http://www.nlm.nih.gov/medlineplus/ency/article/001166.htm> (last updated June 17, 2011).

38. See *id.*

39. See *id.*

40. DENA S. DAVIS, GENETIC DILEMMAS: REPRODUCTIVE TECHNOLOGY, PARENTAL CHOICES, AND CHILDREN’S FUTURES 113 (2d ed. 2010).

41. *Id.* at 113-14.

screening programs].”⁴² Whereas mass spectrometry “measures levels of various metabolites in the blood, the microchips will screen directly for the genetic basis of various disorders.”⁴³ The National Human Genome Research Institute is currently working to reduce the cost of sequencing an entire human genome to \$1,000 by 2014,⁴⁴ from a cost of just under \$8,000 in 2012.⁴⁵

The explosive expansion of new conditions to be screened is controversial. When each condition had to be justified on its own, new screens were added sparingly. Now, there are many pressures to expand screening and no clear criteria for adding new conditions. Rachel Grob identifies a number of factors contributing to the rapid expansion of newborn screening, including “technological innovation, political opportunity, interstate rivalries, and competitive pressure on state programs from private laboratories.”⁴⁶ Advocacy groups, often propelled by families whose own child might have been saved from the consequences of a rare disease if timely screening had been available, push hard to add “their” disease to the screening panel.⁴⁷ Interestingly, parents of children with disorders for which there is currently no medical intervention, such as Fragile X, are equally enthusiastic about routine screening.⁴⁸

Underlying the debate is the fact that almost all newborn screening is done without the informed consent of the parents. In many states, parents can theoretically refuse screening, but because they are rarely told of it beforehand, or told only in very vague terms, this right to refuse is close to meaningless.⁴⁹ A test given without parental consent can only ethically be defended on the grounds of potential benefit to

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42. RACHEL GROB, *TESTING BABY: THE TRANSFORMATION OF NEWBORN SCREENING, PARENTING, AND POLICY MAKING* 8 (Rima D. Apple et al. eds., 2011).
 43. DAVIS, *supra* note 40, at 114.
 44. *Id.*
 45. Omar McCrimmon, *New NIH/NHGRI Grants to Harness Nanoscale Technologies to Cut DNA Sequencing Costs*, NAT’L HUMAN GENOME RES. INST. (Sept. 14, 2012), <http://www.nih.gov/news/health/sep2012/nhgri-14.htm>.
 46. GROB, *supra* note 42, at 3.
 47. See Lainie Friedman Ross & Darrel J. Waggoner, *Parents: Critical Stakeholders in Expanding Newborn Screening*, 161 J. PEDIATRICS 385, 386 (2012).
 48. See PRESIDENT’S COUNCIL ON BIOETHICS, *THE CHANGING MORAL FOCUS OF NEWBORN SCREENING: AN ETHICAL ANALYSIS BY THE PRESIDENT’S COUNCIL ON BIOETHICS* 62 (2008), *available at* http://bioethics.georgetown.edu/pcbe/reports/newborn_screening/Newborn%20Screening%20for%20the%20web.pdf.
 49. See Rachel Grob, *Parenting in the Genomic Age: The ‘Cursed Blessing’ of Newborn Screening*, 25 NEW GENETICS & SOC’Y 159, 159, 163 (2006).

children, backed up by strong evidence. PKU screening fulfills those requirements (assuming that the state follows up with parental education and ensures access to the expensive diet), but screening for other conditions may not. Screening for cystic fibrosis, for example, has been controversial because not everyone agrees that there is a medical advantage to early, presymptomatic diagnosis. However, studies show that early diagnosis of cystic fibrosis prevents malnutrition and improves children's growth and cognitive function.⁵⁰

Screening also has the potential for harm, as can be seen in screening for Fragile X Syndrome, the most common form of inherited intellectual disability. Although Fragile X can have devastating developmental and intellectual consequences, one-third to one-half of all females with the mutation are intellectually normal. Identifying those children could cause unnecessary anxiety in parents or lead them to have mistakenly low expectations of what their daughters can achieve.⁵¹

All large screening programs result in a fair number of false positives that need to be followed by more specific diagnostic tests. Upon additional testing, the result is often a "false alarm." Parents, however, have been shown to continue to feel anxious and to relate differently to their baby even once they have been reassured about the outcome.⁵²

Screening ought to result in a demonstrable benefit, but there is disagreement on what kinds of "benefits" count.⁵³ Saving a child from the devastating effects of PKU is a wonderful benefit. But by what rationale should we screen for disorders for which there is no known medical intervention? Even if the infant itself does not benefit directly, one could argue that there are benefits to the family or to society as a whole. Society, for example, could benefit from knowing more about the incidence of a disease. Of course, this is a research question, and normally we do not allow research on children without parental permission. Parents could benefit from having a heritable disease diagnosed early, before embarking on another pregnancy. Parents (and arguably the child) could also benefit by being spared a "diagnostic odyssey" when the child does become symptomatic.

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50. Rebecca L. Kosciuk et al., *Cognitive Function of Children with Cystic Fibrosis: Deleterious Effects of Early Malnutrition*, 113 PEDIATRICS 1549, 1549 (2004).
51. Donald B. Bailey, Jr. et al., *Ethical, Legal, and Social Concerns About Expanded Newborn Screening: Fragile X Syndrome as a Prototype for Emerging Issues*, 121 PEDIATRICS e693, e696 (2008).
52. See Elizabeth A. Gurian et al., *Expanded Newborn Screening for Biochemical Disorders: The Effect of a False-Positive Result*, 117 PEDIATRICS 1915, 1919-20 (2006).
53. Donald B. Bailey, Jr. et al., *Changing Perspectives on the Benefits of Newborn Screening*, 12 MENTAL RETARDATION & DEVELOPMENTAL DISABILITIES RESEARCH REV. 270, 271 (2006).

From some perspectives, there are few, if any, ethical limits on newborn screening. Duane Alexander, former Director of the National Institute of Child Health and Human Development, considers the principle that one should screen only for disorders for which a treatment exists as an “outmoded” dogma.⁵⁴ Alexander and others call for the development of multiplex screening that would screen newborns for every medically significant genetic marker.⁵⁵ Rather than demanding a rationale for adding a screen, every marker is presumptively “screenable” in the absence of a good reason to exclude it.⁵⁶ The President’s Commission on Bioethics expressed its discomfort with this methodology by terming the practice “newborn profiling.”⁵⁷ In the 1990s, a number of reports argued that the only justification for newborn screening was the possibility of substantial benefit to the child. In the twenty-first century, that perspective seems to be losing out to a wider and not well-delineated notion of “benefit” and of appropriate beneficiaries.⁵⁸

For recessive genetic diseases such as cystic fibrosis, a false positive finding may result in a finding that the baby, while healthy, is a carrier. Knowledge of carrier status can result in inappropriate parental anxiety and serve to reveal a parent’s genetic make-up—all without consent. In this way, newborn screening can act as a kind of proxy genetic testing of the parents. Children who are carriers of a recessive gene will never get sick themselves, so the test does not benefit them. But it does act as unconsented, unsolicited genetic testing of parents⁵⁹ and shares with parents information about the child’s genetic make-up that violates the child’s future privacy. If parents are known not to be carriers of the condition for which their child is a carrier, anxiety about paternity can ensue even though it is possible for the child to have a spontaneous mutation that neither parent carries.⁶⁰

Newborn screening can also warn parents of the genetic risks they run with their next pregnancy, but without consent, such information is a mixed blessing. Rachel Grob argues that “[t]he state’s delivery of unsolicited genetic risk information to women of child-bearing age is a real threat to reproductive autonomy, yet a sustained dialogue about

54. Duane Alexander & Peter C. van Dyck, *A Vision of the Future of Newborn Screening*, 117 PEDIATRICS S350, S352 (2006).

55. *Id.* at S350-54.

56. *See id.* at S352.

57. *See* PRESIDENT’S COUNCIL ON BIOETHICS, *supra* note 48, at 56.

58. Bailey, Jr. et al., *supra* note 53, at 271.

59. *See* Grob, *supra* note 49, at 162.

60. ANTHONY J.F. GRIFFITHS ET AL., AN INTRODUCTION TO GENETIC ANALYSIS (7th ed. 2000), *available at* <http://www.ncbi.nlm.nih.gov/books/NBK21897/>.

this consequence of universal screening is sorely lacking amid the willy-nilly rush to expand state programmes.”⁶¹

When newborn screening was purely for PKU, one could at least make the argument that no parent should risk a baby’s health by refusing the PKU test, although that argument does not obviate the need for parental consent. As time went on, the number of tests exploded and began to include conditions that were not responsive to treatment (e.g., Duchennes muscular dystrophy) or were collected for research purposes only. This is why I label these screens as opportunistic—one begins with a well-established test that the subject expects or that has some sort of rationale, and then piggybacks additional tests onto the same sample. Of course, more tests *should* equal *more* need for consent, especially when the purpose shifts from clinical to research, but in fact all the pressures push in the other direction.

The actual incidence of finding the disease when one screens a general population is relatively low. For example, the incidence of PKU varies greatly across the world; however, in the United States, one of 15,000 infants born every year has the disease.⁶² It is one thing to push an informational folder into the hand of every distracted new parent, but should we really ask a health professional to spend ten or fifteen minutes explaining PKU to each parent when that discussion will prove largely irrelevant 14,999 times out of 15,000? With the relative ease of adding one more test onto the panel, informed consent becomes more difficult to support.

One way to encourage more meaningful parental involvement in newborn screening (and perhaps to alleviate the anxiety of a false positive result) is to give information during the prenatal period when parents have time to assimilate it and to ask questions. The New England Regional Genetics Group, for example, produces a simple, informative brochure that can be customized for the different states and made available in many languages.⁶³ The brochure does not, however, tell parents that they have the right to refuse screening, nor does it inform them that not every test produces “actionable” information relevant to their baby’s health.⁶⁴

Currently, Internet information could be an important resource for new and expectant parents. The Internet is an especially appropriate venue for public health education such as information about newborn screening, which delivers generally applicable information and typically

61. Grob, *supra* note 49, at 162-63.

62. See Nat’l PKU Alliance, *PKU Facts*, NAT’L PKU ALLIANCE, <http://www.npkua.org/index.php/pku-facts> (last visited Jan. 13, 2013).

63. *New England Newborn Screening Brochure*, NEW ENGLAND RELATIONAL GENETICS GROUP, INC., <http://www.nergg.org/nbsbrochures.php> (last visited Jan. 17, 2013).

64. *Id.*

does not require “personal messaging.”⁶⁵ Araia and Potter analyzed two sets of guidelines developed in the United States (in 2000 and 2006) and identified fourteen “messages” that the guidelines recommended be communicated to parents about newborn screening.⁶⁶ Tellingly, none of the fourteen involved parental consent. Using the fourteen recommendations as well as their own addition of informed consent, Araia and Potter conducted a systematic search of public websites of newborn screening programs in the United States and Canada in 2008.⁶⁷ Sixteen percent of US sites and none of the Canadian sites included information about policies for storage and secondary (research) use of samples.⁶⁸ Seventy-eight percent of the US sites but only 11 percent of the Canadian sites presented information about parental consent or refusal.⁶⁹ Over 80 percent of the sites presented the benefits of newborn screening, while fewer than 60 percent included information about the risks (e.g., false positives).⁷⁰

Another way for parents to receive information about newborn screening during the prenatal period is to read about it in the plethora of popular pregnancy manuals available today. A nonscientific sampling of what is available at a local Barnes & Nobles yielded mixed results. The three manuals for sale all mentioned newborn screening. The most disappointing was *The Mommy Docs’ Ultimate Guide to Pregnancy and Birth*, which provided four sentences couched entirely in the passive mood as if parents were totally disengaged from the process: “Your baby will be screened for a panel of diseases before you leave the hospital The results of these tests will be sent to your pediatrician within a month.”⁷¹

Great Expectations: Your All-in-One Resource for Pregnancy and Childbirth did somewhat better, mentioning that the array of tests differed by state and ending with “[i]f you would like to know more about the tests, don’t be shy about asking your baby’s pediatrician for more information.”⁷² I was disappointed that the hugely popular *What to Expect When You’re Expecting*, nearly in its 600th week on the New

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65. Mollyann Brodie et al., *Health Information, the Internet, and the Digital Divide*, 19 HEALTH AFFAIRS 255, 262 (2000).
66. Makda H. Araia & Beth K. Potter, *Newborn Screening Education on the Internet: A Content Analysis of North American Newborn Screening Program Websites*, 2 J. COMMUNITY GENETICS 127, 129 (2011).
67. *Id.* at 128-29.
68. *Id.* at 129.
69. *Id.* at 129-30.
70. *Id.* at 129.
71. YVONNE BOHN ET AL., THE MOMMY DOCS’ ULTIMATE GUIDE TO PREGNANCY AND BIRTH 287 (2011).
72. SANDY JONES ET AL., GREAT EXPECTATIONS: YOUR ALL-IN-ONE RESOURCE FOR PREGNANCY & CHILDBIRTH 435 (2004).

York Times Book Review best seller list,⁷³ is extremely vague, talking about life-threatening diseases without naming any and stating that “early diagnosis and intervention can make a tremendous difference in the prognosis,” without giving any idea of what kind of prognosis that might be.⁷⁴ *What to Expect* does refer parents to useful websites for more information, including one that informs the reader whether her state screens for the conditions recommended by the March of Dimes.⁷⁵ I had to go online to satisfy my curiosity about *Our Bodies, Ourselves: Pregnancy and Birth*, part of the series that began in 1971 with the explicit goal of empowering women through information.⁷⁶ Not surprisingly, *Our Bodies, Ourselves* gave the most detailed information, including the fact that some states include HIV screening in their panel of tests.⁷⁷ It was the only book to tell women that they could refuse screening or even request additional tests.⁷⁸ None of the books mentioned that newborn screening could pick up information with no health consequences, such as carrier status for recessive genetic diseases.

In addition to screening newborns without parental consent, some states have also retained the dried blood spots (preserved from the newborns’ heelsticks) and used them for research purposes, again without consent. Michigan, for example, now has “almost four million stored blood spots potentially available for research representing state birth cohorts from 1984 to the present.”⁷⁹ These deidentified blood spots were used in ten studies without the consent of the parents.⁸⁰ This research use of existing tissue samples is considered acceptable under the federal guidelines governing research with human subjects.⁸¹ In February

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73. *Best Sellers: Paperback Advice & Misc.*, N.Y. TIMES, <http://www.nytimes.com/best-sellers-books/2013-01-20/paperback-advice/list.html> (last visited Jan. 18, 2013).
74. HEIDI MURKOFF & SHARON MAZEL, *WHAT TO EXPECT WHEN YOU’RE EXPECTING* 297 (4th ed. 2008).
75. *Id.*
76. See Rebecca S. Dresser, *What Bioethics Can Learn from the Women’s Health Movement*, in *FEMINISM AND BIOETHICS: BEYOND REPRODUCTION* 144, 145 (Susan M. Wolf ed., 1996).
77. THE BOSTON WOMEN’S HEALTH COLLECTIVE, *OUR BODIES, OURSELVES: PREGNANCY AND BIRTH* 246 (2004).
78. *Id.*
79. Ann Mongoven & Harry McGee, *IRB Review and Public Health Biobanking: A Case Study of the Michigan BioTrust for Health*, 34 *IRB: ETHICS & HUMAN RES.* 11, 12 (2012).
80. *Id.*
81. *Guidance on Research Involving Coded Private Information or Biological Specimens*, U.S. DEP’T OF HEALTH & HUM. SERVS. (Oct. 16, 2008), <http://www.hhs.gov/ohrp/policy/cdebiol.html>.

2010, however, in response to a lawsuit initiated by parents, the State of Texas was forced to incinerate millions of cached and deidentified blood spots collected since 2002; parents successfully claimed that retaining the samples without their knowledge or consent constituted an illegal search and seizure.⁸² In 2009, Texas began a program allowing parents to opt out of retention.⁸³

In Michigan, the BioTrust for Health was inaugurated in 2009.⁸⁴ The formation of the BioTrust changed the paradigm for use of blood spots in the state. Before the BioTrust, the spots were collected primarily for screening, stored in large part for purposes of quality control, and used (in deidentified form) only “incidentally” for research.⁸⁵ After the inauguration of the BioTrust, research became one of the primary goals.⁸⁶ The Michigan Department of Community Health Institutional Review Board (IRB) determined that parental permission was required before stored samples could be used for research.⁸⁷ Although deidentifying samples addressed parental privacy concerns, other concerns also existed, including the possibility that the state would use samples in research not consonant with individual parents’ values.⁸⁸ It will be interesting to see if and how this more rigorous standard for parental consent to retain and use blood samples for research purposes will change the standards for consenting to screening alone. The IRB wondered if “the explicit request to consent to research might make new parents question why they were not asked for their consent to take blood from their child in the first place.”⁸⁹

In sum, the ease with which new screens can be added threatens parental rights to be aware of and consent to the medical tests conducted on their children and the research their children take part in. Lack of consent is doubly sad because parents would overwhelmingly grant consent if they were asked. In Maryland, where consent is required, a survey found that only 27 out of approximately 50,000 mothers declined screening but that more than half of those mothers thought it important that they be asked.⁹⁰

82. Ann Waldo, *The Texas Newborn Bloodspot Saga has Reached a Sad—and Preventable—Conclusion*, GENOMICS L. REP. (Mar. 16, 2010), <http://www.genomicslawreport.com/index.php/2010/03/16/the-texas-newborn-bloodspot-saga-has-reached-a-sad-and-preventable-conclusion/>.

83. *Id.*

84. Mongoven & McGee, *supra* note 79 at 11.

85. *See id.* at 11-12.

86. *Id.* at 12.

87. *Id.*

88. *Id.* at 13.

89. *Id.*

90. *See* Ruth Faden et al., *A Survey to Evaluate Parental Consent as Public Policy for Neonatal Screening*, 72 AM. J. PUB. HEALTH 1347, 1350 (1982).

IV. NONINVASIVE PRENATAL DIAGNOSIS

Finally, I will consider noninvasive testing for Down Syndrome (DS) based on cell-free fetal nucleic acids. DS is a chromosomal abnormality consisting of an extra chromosome on the twenty-first pair, often termed Trisomy 21.⁹¹ DS is one of the most common genetic birth defects.⁹² Children with DS often have physiological problems requiring surgery, such as malformed hearts or digestive system blockages.⁹³ The majority of people with DS have hearing and vision problems.⁹⁴ They always have distinguishing facial characteristics and some degree of intellectual disability.⁹⁵ Although prenatal screening and testing for DS was one of the earliest available tests, knowing that a fetus has DS does not reveal how severe the condition will be.⁹⁶ Some children with DS graduate from high school, hold down jobs, live semi-independently, and even marry. Others are much more severely affected.⁹⁷

The standard practice for screening and testing pregnant women for fetal chromosomal abnormalities such as DS is a mix of noninvasive and invasive screenings and tests throughout the first and second trimesters.⁹⁸ An array of screening tools based on maternal blood samples provides each pregnant woman with an individual risk assessment, but they are not diagnostic and will not detect all chromosomal abnormalities.⁹⁹ Invasive testing—chorionic villus sampling (CVS) or amniocentesis—is extremely accurate, but carries a small but significant risk of miscarriage.¹⁰⁰ Ironically, while the risk of trisomy increases with maternal age,¹⁰¹

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91. *Down Syndrome*, MARCH OF DIMES, http://www.marchofdimes.com/baby/birthdefects_downsyndrome.html (last updated July 2009) [hereinafter *March of Dimes*].
92. *Id.*
93. *Id.*
94. *Id.*
95. *See id.*
96. *Id.*
97. *See id.*
98. American College of Obstetricians & Gynecologists, *ACOG Practice Bulletin: Clinical Management Guidelines for Obstetrician-Gynecologists Number 77: Screening for Fetal Chromosomal Abnormalities*, 109 OBSTETRICS & GYNECOLOGY 217, 219 (2007) [hereinafter *ACOG Bulletin 77*].
99. *Id.*
100. Amniocentesis is a procedure used to obtain a small sample of the amniotic fluid that surrounds the fetus during pregnancy. The fluid is sent to a genetics lab so that the cells can grow and be analyzed. Results are usually available in about 10 days to two weeks, depending on the lab. Chorionic villus sampling takes fetal cells directly from the placenta.
101. *March of Dimes*, *supra* note 91.

maternal age is also associated with lessened fertility; it is precisely those women with the highest risk of chromosomal abnormality who can least afford to lose a wanted pregnancy. Invasive testing is also time-consuming and labor-intensive. Therefore, an early, noninvasive, highly accurate test for DS is one of the “holy grails” of prenatal diagnosis.¹⁰²

In October 2011, the company Sequenom announced that it was releasing a test that detects DS through cell-free fetal DNA circulating in maternal blood during the first trimester of pregnancy.¹⁰³ Natera, a company that already offers noninvasive fetal paternity testing, is also conducting trials for noninvasive testing for DS.¹⁰⁴ Sequenom claims that its test “is aimed at the estimated 750,000 pregnancies at high risk for Down Syndrome annually in the U.S.,”¹⁰⁵ but as the cost of testing comes down, there is no reason to reserve it only for pregnancies at high risk for DS. Although Sequenom’s test is currently limited to DS and is less accurate for other types of chromosomal abnormalities, it has a 98.6 percent success rate in accurately identifying DS pregnancies, with a 0.20 percent false-positive rate.¹⁰⁶ While the study authors concluded that conventional invasive testing should follow this test,¹⁰⁷ the hope for the near future is that invasive tests will be rendered unnecessary in most cases.¹⁰⁸

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102. Mara Hvistendahl, *Will Gattaca Come True?*, SLATE (Apr. 27, 2012, 7:30 AM), http://www.slate.com/articles/health_and_science/future_tense/2012/04/noninvasive_prenatal_diagnostic_tests_ethics_abortion_and_insurance_coverage_single.html.
 103. Cell-free fetal DNA is considered a biomarker of a current pregnancy that is detectable during the first trimester in maternal blood. Intact fetal cells are detectable in maternal blood for decades after pregnancy. Cell-free DNA, however, is not detectable within minutes of delivery. These cells are “easily extracted and quantified using real-time polymerase chain reaction (PCR) amplification techniques.” Diana W. Bianchi et al., *Insights into Fetal and Neonatal Development Through Analysis of Cell-Free RNA in Body Fluids*, 86 EARLY HUM. DEV. 747, 747 (2010).
 104. *Non-invasive Prenatal Testing*, NATERA, <http://www.natera.com/non-invasive-prenatal-testing.html> (last visited Jan. 17, 2013).
 105. Ryan Flinn, *Sequenom to Sell Down Syndrome Test 2 Years After Pullback*, BLOOMBERG (Oct. 17, 2011, 4:39 PM), <http://www.bloomberg.com/news/2011-10-17/sequenom-to-sell-down-syndrome-test-2-years-after-pullback.html>.
 106. Glenn E. Palomaki et al., *DNA Sequencing of Maternal Plasma to Detect Down Syndrome: An International Clinical Validation Study*, 13 GENETICS MEDICINE 913, 913 (2011).
 107. *See id.* at 919.
 108. Vardit Ravitsky, *Non-Invasive Prenatal Diagnosis: An Ethical Imperative*, 10 NATURE REV. GENETICS 733, 733 (2009); Dagmar Schmitz et al., *An Offer You Can’t Refuse? Ethical Implications of Non-Invasive Diagnosis*, 10 NATURE REV. GENETICS 515, 515 (2009).

There are, of course, enormous emotional and ethical issues attached to prenatal diagnosis. While an oft-heard statistic is that 90 percent of pregnancies diagnosed with DS are terminated, that figure reflects a population that had already agreed to go ahead with testing, presumably with at least some openness to termination. Others choose not to test because they would not terminate. When the gold standard for detection of DS is an invasive test (i.e., CVS or amniocentesis), informed consent is a *sine qua non*. The risk of miscarriage makes consent crucial, as each woman will evaluate and balance the risks in an individual way. But, it obviously would be unthinkable to perform CVS or amniocentesis without consent because it is an invasive, stand-alone procedure that cannot be piggybacked onto something else. A woman undergoing an amniocentesis *knows* she is having an amniocentesis. Marteau and colleagues report that, in one group of over 200 women, 29 percent who had an Alpha Fetoprotein screening test denied having had it (presumably because they had not been aware of being tested), whereas all of the women who underwent amniocentesis appeared to have given truly informed consent.¹⁰⁹ “Confronted with a long needle or a transvaginal probe, few, if any, women will undergo either procedure without understanding that something serious is happening.”¹¹⁰ Thus, CVS and amniocentesis are the focus of thoughtful, often anguished decision-making. Weighing the risk of having a baby with DS versus the risk of losing a healthy fetus forces couples to think about DS and what a child with it would mean for their family.

I am not extolling anguish for its own sake—there is enough anguish in the world already—and I think that a decisive test for DS that is noninvasive and free of risk is a wonderful thing. It is excellent that women will be able to focus on the question of testing for DS without the risk of miscarriage. However, I worry that this will become another opportunistic test often performed without informed consent.

It also appears that many women receive prenatal screening (the blood tests used within the first and second trimesters of pregnancy to estimate a woman’s risk of having a baby with certain genetic defects) without proper consent.¹¹¹ In addition to Marteau’s study, a German study found that 16 percent of women either had not given consent or could not remember giving consent.¹¹² A French study found that nearly half the women who had undergone prenatal screening were “unin-

109. Theresa M. Marteau et al., *Factors Influencing the Uptake of Screening for Open Neural-Tube Defects and Amniocentesis to Test for Down’s Syndrome*, 96 BRIT. J. OBSTETRICS & GYNAECOLOGY 739, 739-40 (1989).

110. Henry T. Greely, *Get Ready for the Flood of Fetal Gene Screening*, 469 NATURE 289, 291 (2011).

111. Schmitz et al., *supra* note 108.

112. *Id.*

formed” about the procedure.¹¹³ But it is difficult to know what to make of this. Pregnancy is a busy time, and prenatal care involves many tests to protect and monitor the health of the mother and her fetus. Thus, it is possible that many women understood and consented to a test and then forgot about it when the results were of no concern. However, a recent study of American obstetricians found that a surprisingly large number of pregnant women age thirty-five and over refused screening, ranging from almost 20 percent of women in the West and Northeast, to more than 30 percent in the South.¹¹⁴ That result suggests that women did make a decision and felt comfortable going against “routine.”¹¹⁵

Scholars differ on whether noninvasive prenatal diagnosis (NIPD) for DS will lead to more or less robust informed consent. De Jong and colleagues argue that NIPD testing does not present a greater challenge to ensuring a proper consent process¹¹⁶:

[I]n current practice information, counselling [sic] and consent are often inadequate[] However, as long as NIPD testing will be offered for the same range of abnormalities as in the present[] approach to prenatal screening, there is no reason to assume that these problems will be larger than they already are.¹¹⁷

Greely worries that without the lengthy counseling necessitated by an invasive procedure, “how can we ensure that parents understand what they are consenting to? Already some who get results from blood-based screening . . . are shocked to learn they ever agreed to the test.”¹¹⁸ In other words, so-called “informed consent” was not consent at all. Van den Heuvel and colleagues conducted the first study to assess how practitioners view the consent process for noninvasive as opposed to invasive testing; they concluded that practitioners may view them differently, and that “[t]here is potential for the introduction of NIPD to undermine women making informed choices in the context of prenatal diagnostic testing for conditions like DS.”¹¹⁹

113. *Id.*

114. See Deborah A. Driscoll et al., *Screening for Down Syndrome: Changing Practice of Obstetricians*, 200 AM. J. OBSTETRICS AND GYNECOLOGY 459.e1, 459.e4 (2009).

115. See *id.* at 459.e4-e5.

116. Anita de Jong et al., *Non-Invasive Prenatal Testing: Ethical Issues Explored*, 18 EUR. J. HUM. GENETICS 272, 273 (2010).

117. *Id.*

118. Greely, *supra* note 110, at 291.

119. Ananda van den Heuvel et al., *Will the Introduction of Non-Invasive Prenatal Diagnostic Testing Erode Informed Choices? An Experimental Study of Health Care Professionals*, 78 PATIENT EDUC. & COUNSELING 24, 24 (2010).

Ravitsky, however, looks forward to the time when counselors will be able to devote more time to discussing “the possible results of the test—and the alternatives open to women and their families—rather than spend[ing] a substantial amount of time and effort discussing the risk inherent in the test.”¹²⁰ She believes that NIPD would promote autonomous decision making by shifting the focus where it belongs.¹²¹ And Deborah Driscoll, a geneticist and chair of the University of Pennsylvania, Perelman School of Medicine’s Department of Obstetrics and Gynecology, where the new test was rolled out in August 2012, said, “I think one of the concerns that some geneticists and ethicists have is that we want to be sure that women give informed consent.”¹²² She states that “this [should] not [be] viewed as a routine laboratory test,” and that “[e]very physician or counselor that offers this [should] explain[] to the patient what the test is for, what are the limitations for the test and what it can potentially disclose.”¹²³

At issue here is something I will call the “crossroads effect.” At present, a fairly common attitude appears to be that maternal serum screening (the so-called “triple” and “quadruple” tests offered in the first and second trimesters)¹²⁴ does not require a robust consent process. Although the American College of Obstetricians and Gynecologists, for example, directs healthcare providers to make extensive information about screening tests available to patients “so that they can make informed decisions,”¹²⁵ the empirical studies cited elsewhere in this essay show that the reality can be quite different. This may well be, at least in part, because no final decisions will be acted upon in response to the screening test alone. A positive screen becomes a crossroads moment at which a woman must decide whether or not to undergo invasive diagnostic testing. Because only about 5 percent of pregnancies will have a positive screen result necessitating further decisions,¹²⁶ the attitude of many busy practitioners may well mirror the attitude I posited earlier about consent for PSA testing. That is the moment when routine changes into individualized decision making.

I fear that *screening* without informed consent will become *testing* without informed consent in a fairly seamless way. The threat to autonomy comes from opportunistic testing combined with pressures of

120. Ravitsky, *supra* note 108, at 733.

121. *Id.*

122. Taunya English, *Docs Offer First Trimester Down Syndrome Test*, NEWSWORKS (Aug. 15, 2012), http://www.newsworks.org/index.php?option=com_flexicontent&view=items&id=42975:docs-offer-

123. *Id.*

124. *ACOG Bulletin* 77, *supra* note 98, at 224.

125. *Id.* at 219.

126. *Id.* at 218.

time and money and extruded through the trend toward routinization that seems pervasive in medicine.¹²⁷ Once routinized, clinicians will portray NIPD tests, and women will experience them, as a routine and normal part of prenatal care.¹²⁸ “This may lead to normalization of uptake, ranging from a rather thoughtless uptake to women feeling socially pressurized to be tested.”¹²⁹

In sum, noninvasive prenatal diagnosis for DS can be a boon to women’s autonomy, allowing them to think clearly about motherhood and disability without the distractions of an invasive and minimally risky test. It will also allow women who choose to terminate to do so in the first trimester when it is safer, easier, and cheaper. But that advance in autonomy could be offset if testing is not accompanied by the opportunity for thoughtful informed consent.

V. CONCLUSION

The bioethics movement was born as a full-throated defense of patient empowerment. Respect for persons meant respect for the voluntary, informed choice of the competent patient, the better to support personal autonomy. The challenges in the twentieth century were lack of information and a paternalistic medical profession. In the twenty-first century, the challenge to autonomy may be a combination of opportunistic testing, new technology, and lack of time.

127. See generally John B. McKinlay, *From “Promising Report” to “Standard Procedure”: Seven Stages in the Career of a Medical Innovation*, in 8 TECHNOLOGY & THE FUTURE OF HEALTH CARE: MILBANK READER 233, 235-54 (John B. McKinlay ed., 1982).

128. de Jong et al., *supra* note 116, at 273.

129. *Id.* at 273-74.